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(19)

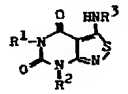
(54) 3-AMINOISOTHIAZOLO-[3,4-d]-PYRIMIDINES

(71) We, BASF AKTIENGESELLSCHAFT, a German Joint Stock Company of 6700 Ludwigshafen, Federal Republic of Germany, do hereby declare the invention, for which we pray that a Patent may be granted to us, and the method by which it is to be performed to be particularly described in and by the following statement:—

The present invention relates to 3-aminoisothiazolo-[3,4-d]-pyrimidines and to a process for preparing such 3-aminoisothiazolo-[3,4-d]-pyrimidines.

The ring system of isothiazolo-[3,4-d]-pyrimidines was described for the first time by K. Hartke and L. Peshkar in Archiv der Pharmazie, *301*, 611 to 621. Starting from malononitrile and dithio or thio esters there are obtained in a condensation reaction the salts of 2-mercapto-1-cyano-acrylonitriles which by reaction with chloramine give 3-amino - 4 - isothiazolecarbonitriles; from the latter there are obtained by reaction with orthoformic acid esters and acetic anhydride 3 - [ethoxymethylene] - amino - 4 - isothiazolecarbonitriles which can be cyclized with ammonia to give isothiazolo-[3,4-d]-pyrimidines.

We have now found 3-aminoisothiazolo-[3,4-d] - pyrimidines of the general formula:—



(I)

in which R^1 and R^2 are, each independently, hydrogen, a linear or branched, saturated or unsaturated alkyl group of one to six carbon atoms which optionally may be substituted, an aralkyl or unsubstituted or substituted cycloaliphatic, heterocyclic or aromatic radical, and R^3 is hydrogen, sulfonyl or carboxylic acyl.

Examples of alkyl for R^1 and R^2 are methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, and n-hexyl; examples of unsaturated alkyl are allyl or methallyl and examples of substituted alkyl are γ-methoxypropyl, tert-butoxypropyl and β-dimethylaminoethyl.

Benzyl, phenylethyl and γ-phenylpropyl are suitable aralkyls.

The cycloaliphatic radicals are preferably derived from cycloaliphatic rings having three to six carbon atoms in the ring and may be substituted by alkyl such as methyl or ethyl. Cyclohexyl or cyclohexyl bearing methyl as a substituent are particularly suitable.

Examples of heterocyclic radicals are the furyl and thienyl radicals which may be substituted in conventional manner.

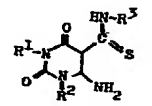
The preferred aromatic radical is the phenyl group which may bear chloro, bromo, methoxy, ethoxy, methyl or ethyl as substituents, such as p-chlorophenyl, p-methylphenyl and p-methoxyphenyl.

Suitable sulfonyl radicals for R^3 include alkylsulfonyl, preferably of one to four carbon atoms, cycloalkylsulfonyl, unsubstituted or substituted arylsulfonyl, aralkylsulfonyl or heteroarylsulfonyl. Specific examples are methylsulfonyl, ethylsulfonyl, propylsulfonyl, butylsulfonyl, cyclohexylsulfonyl, benzylsulfonyl, phenylethylsulfonyl, phenylsulfonyl, chlorophenylsulfonyl, dichlorophenylsulfonyl, nitrophenylsulfonyl, methylphenylsulfonyl, dimethylphenylsulfonyl and thienylsulfonyl.

Carboxylic acyl radicals for R^3 include substituted or unsubstituted alkanoyl radicals preferably of one to seven carbon atoms, such as acetyl, propionyl, butyryl, caproyl, hexanoyl, capryloyl, β-ethylhexanoyl, chloroacetyl, bromoacetyl, α-chloropropionyl, β-chloropropionyl, γ-chloro-n-butyryl and γ-bromoisovaleroyl; aralkanoyl radicals such as phenylacetyl, tolylacetyl, methoxyphenylacetal, chlorophenylacetyl or dichlorophenylacetal, alkoxycarbonyl or aroxycarbonyl radicals such as methoxycarbonyl, ethoxycarbonyl, propoxycarbonyl, butoxycarbonyl, or phenoxycarbonyl, substituted or unsubstituted aroyl, such as

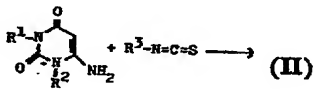
benzoyl, or benzoyl, naphthoyl or phenanthronyl bearing chloro, bromo, nitro, methoxy, ethoxy or methyl as substituents, or a heterocyclic radical such as furoyl or thienoyl.

The invention also relates to a process for the production of 3-aminoisothiazolo-[3,4-d]-pyrimidines of formula I wherein a 4-aminouracil-5-carboxylic thioamide of the formula (II):



in which
R^1, R^2 and R^3 have the above meanings is oxidatively cyclized.

4 - Aminouracil - 5 - carboxylic thioamides of the formula (II) may be prepared in accordance with German Patent Specification 21 50 686 from 4-aminouracils by reaction with a sulfonyl or carboxylic acyl isothiocyanate according to the equation:—



(II)

where R^1, R^2 and R^3 are the corresponding substituents. Reaction of the 4-aminouracils (which are prepared by prior art methods, for example J. Org. Chem. *16* (1951), 1879 to 1890) with a sulfonyl or carboxylic acyl isothiocyanate which are also prepared by prior art methods for example German Printed Application DAS 1,183,492 and Houben-Weyl, "Methoden der organischen Chemie", 4th edition, *9*, 879, G Thieme, Stuttgart, 1955, and J. Org. Chemistry, 29 (1964), 2261 and Pharmaz. Zentralhalle 197, (1968). page 277) is carried out at temperatures of from 0° to 200° C expediently in a solvent and the reaction product is processed by a conventional method.

The reaction of the 4-aminouracil with the sulfonyl or carboxylic acyl isothiocyanate is carried out conveniently at temperatures of from 10° to 200° C, preferably from 20° to 100° C, in a solvent or diluent inert to the reactants. These include for example 1,2-dimethoxyethane, tetrahydrofuran, dioxane, formamide, dimethylformamide, dimethylacetamide, N-methylpyrrolidine, tetramethylenesulfone, benzene, toluene, chlorobenzene, benzonitrile and acetonitrile. The reaction may also be carried out without an added solvent using an excess of allyl isothiocyanate.

For example 0.1 mole of a 4 aminouracil of the said formula may be dissolved or suspended at ambient temperature in a solvent or diluent and then while stirring at least 0.1 mole of sulfonyl or carboxylic acyl isothiocyanate is added. Almost invariably an exothermic reaction commences immediately. To complete the reaction the whole is heated for from half an hour to three hours, preferably from one hour to two hours, at 40° to 80° C. The reaction product, which often is sparingly soluble, usually crystallizes out on cooling; if necessary some of the solvent may be distilled off at subatmospheric pressure or ether, ligroin, cyclohexane or water may be added to the concentrated solution in order to achieve or complete the separation.

The reaction mixture is processed by a conventional method, for example by suction filtration of the precipitate, washing for example with water, an alcohol, an ether, ligroin or cyclohexane, and drying at subatmospheric pressure.

When carrying out the reaction with an excess of allyl isothiocyanate (the 4-aminouracil being introduced for example into about 4 to 8 times the molar amount of the same advantageously with stirring and after the exothermic reaction has subsided the whole is heated for another one hour to three hours at 40° to 80° C) it is advantageous to use for the isolation of the reaction product a diluent which does not dissolve it, for example an aliphatic or cycloaliphatic hydrocarbon. The reaction product is then obtained in a form in which it can easily be suction filtered; unreacted isothiocyanate can be recovered from the filtrate by fractionation.

Oxidative cyclization of the 4-aminouracil-5-carboxylic thioamides is conveniently carried out in the presence of an inert solvent and/or suspension agent at a temperature of from 0° to 180° C preferably at from 10° to 120° C.

Examples of oxidizing agents which effect cyclization are hydrogen peroxide and derivatives thereof, e.g. Caro's acid, persulfuric acid, peracetic acid, perboric acid, perphthalic acid or perbenzoic acid, bromine, chlorine, sulfuryl chloride, sulfur trioxide, sulfur dichloride, chromic acid, hypochlorous acid, perchloric acid, ozone or concentrated sulfuric acid.

Solvents and/or suspension agents which are inert to the reactants are conveniently used. Thus for example water, lower fatty acids, alkanols, ethers, halohydrocarbons, lower fatty acid esters, amides of lower fatty acids and mineral acids may be used as solvents. The process may also be carried out in the presence of a base, for example pyridine, sodium hydroxide or potassium hydroxide. Suitable reaction media include: acetic acid, propionic acid, chloroform, dimethylformamide, dimethylsulfoxide, water and sulfuric acid.

The preferred oxidizing agents are concentrated sulfuric acid (which in excess may

be used as a solvent as well), bromine (particularly in solution in chloroform or dimethylformamide) and about 50% hydrogen peroxide solution using dimethylformamide as an additional solvent.

To carry out the process the 4-aminouracil-5-carboxylic acid thioamide is conveniently dissolved or suspended in the solvent used and then the oxidizing agent is added to it. It is advantageous to cool the reaction mixture and if necessary to heat it for a short time after the initial exothermic reaction has subsided. For each mole of 4-aminouracil-5-carboxylic thioamide the amount of oxidizing agent used is generally from one to twenty times and preferably from once to twice the equivalent amount.

Processing causes no difficulties and depends on the oxidizing agent, solvent and/or suspension agent used. When an acid is used as the oxidizing agent or reaction medium or when an oxidizing agent is used which forms an acid under the reaction conditions, a convenient procedure is to add the reaction mixture to ice-water and then to add alkaline substances such as caustic soda solution, caustic potash solution, aqueous ammonia, sodium carbonate or potash until the reaction mixture is neutral. The isothiazolo-[3,4-d]-pyrimidine thus precipitated may be separated for instance by filtration or centrifuging.

When a mineral acid, particularly sulfuric acid, is used as oxidizing agent and/or suspension agent elimination of the R^3 radical may take place at the same time as oxidative cyclization, a 3-aminoisothiazolo-[3,4-d]-pyrimidine thus being obtained which has no substituent on the amine group.

Naturally the R^3 radical may also be eliminated in a separate reaction after cyclization has taken place. Elimination can be effected not only with acids, for example sulfuric acid and hydrochloric acid, but also with bases, for example caustic soda solution and caustic potash solution.

Examples of suitable sulfonyl and carboxylic acyl isothiocyanates as starting compounds are:—

p-toluenesulfonylisothiocyanate,
benzenesulfonylisothiocyanate,
o-toluenesulfonylisothiocyanate,
o-chlorobenzenesulfonylisothiocyanate,
m-chlorobenzenesulfonylisothiocyanate,
p-chlorobenzenesulfonylisothiocyanate,
3,4-dichlorobenzenesulfonylisothiocyanate,
thiophene-2-sulfonylisothiocyanate,
cyclohexanesulfonylisothiocyanate,
methanesulfonylisothiocyanate,
ethanesulfonylisothiocyanate,
benzoylisothiocyanate,
4-methoxybenzoylisothiocyanate,
p-chlorobenzoylisothiocyanate,
p-nitrobenzoylisothiocyanate,
m-methoxybenzoylisothiocyanate,
o-methylbenzoylisothiocyanate,
m-methylbenzoylisothiocyanate,
p-methylbenzoylisothiocyanate,
3,5-dimethylbenzoylisothiocyanate,
2,6-dichlorobenzoylisothiocyanate,
2,4,6-trimethylbenzoylisothiocyanate,
3,4,5-trimethoxybenzoylisothiocyanate,
thienoylisothiocyanate,
α-naphthoylisothiocyanate,
β-naphthoylisothiocyanate,
3-phenanthroylisothiocyanate,
phenylacetylisothiocyanate,
m-tolylacetylisothiocyanate,
p-tolylacetylisothiocyanate,
m-methoxyphenylacetylisothiocyanate,
p-methoxyphenylacetylisothiocyanate,
p-chlorophenylacetylisothiocyanate,
carbomethoxyisothiocyanate,
carbethoxyisothiocyanate,
carbobutoxyisothiocyanate,
phenoxycarbonylisothiocyanate,
acetylisothiocyanate,
propionylisothiocyanate,
butyrylisothiocyanate,
n-caproylisothiocyanate,
n-capryloylisothiocyanate,
chloroacetylisothiocyanate,
α-chloropropionylisothiocyanate,
β-chloropropionylisothiocyanate,
α-bromoisobutyrylisothiocyanate,
γ-chloro-n-butyrylisothiocyanate and
α-bromoisovaleroylisothiocyanate.

The 3 - aminoisothiazolo - [3,4-d]-pyrimidines obtained according to the invention are valuable intermediates for the production of dyes, pesticides and medicaments. Compounds in which R^3 is hydrogen are particularly important in this respect. For example, they are also of interest as potential purine antimetabolites.

The 3 - aminoisothiozolo - [3,4-d]-pyrimidines of the invention have valuable therapeutic properties for example as diuretics or as anti-inflammation agents and they may also be used as fungicides. Accordingly, the invention includes within its scope pharmaceutical compositions containing a novel compound according to the invention together with a pharmaceutically-acceptable carrier or diluent and also fungicidal compositions comprising such a compound together with a carrier or diluent.

The following compounds in particular have a good biological action: 3-amino-5, 7 - dimethylisothiazolo - [3,4-d] - pyrimidinedione - (4,6), 3 - [N - carbethoxy]-amino - 5,7 - dimethylisothiazolo - [3,4-d]-pyrimidinedione - (4,6), 3 - [N - p - toluenesulfonyl] - amino - 7 - ethylisothiazolo-[3,4-d] - pyrimidinedione - (4,6) and 3-amino - 5,7 - dipropylisothiazolo[-3,4-d]-pyrimidinedione-(4,6).

Formulations with the compounds of the invention as active ingredients may be ob-

tained by conventional methods depending on the type of application required.

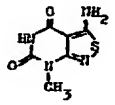
Particular importance attaches to compounds of the formula (I) in which:

R^1 is hydrogen, alkyl of one to four carbon atoms, benzyl, phenylethyl, cyclohexyl or phenyl which may bear chloro, methyl or methoxy as a substituent;
R^2 denotes, except for hydrogen, the same radicals as R^1 and additionally alkoxyalkyl of a total of up to six carbon atoms; and
R^3 has the above meanings.

For use as diazo components compounds having alkyl as R^1 and R^2 and particularly methyl, are preferred; R^3 is naturally hydrogen in this case.

The following examples, in which parts and percentages are by weight unless otherwise stated, illustrate the invention.

Example 1.



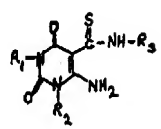
354 parts of 3 - methyl - 4 - aminouracil-5 - [N - (p - toluene sulfonyl)] - carboxylic thioamide is gradually introduced into 1000 parts of concentrated sulfuric acid while stirring at a temperature of about 75° C and in the course of thirty minutes. Reaction immediately takes place as evidenced by the escape of sulfur dioxide. When all has been added the mixture is stirred for another two hours at 80° C. The clear solution is cooled and poured onto about 5000 parts of ice-water. The deposited colorless solid is suction filtered, washed with water until neutral and then dried in vacuo at 80° C. Chromatographic and infra-red spectroscopic analysis show the product to be identical with a sample recrystallized from dimethylformamide. The yield is 173.5 parts, which is 88% of theory. Melting point: 360° to 362° C. Analysis: $C_6H_6N_4O_2S$: molecular weight 198.14.

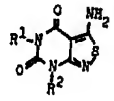
calculated:
C 36.4 H 3.1 N 28.3 O 16.1 S 16.1
found:
36.3 3.3 27.9 16.3 16.4

The compounds set out as Examples 2 to 7 in Table 1 may be prepared by the process described in Example 1, the sulfonyl or acyl radical being eliminated in each case under the reaction conditions. The following abbreviations are used in Table 1:

Ex = Example No.
Y = Yield
m.p. = melting point
Rec. = recrystallized from
Emp. = empirical formula and molecular weight
c = calculated
f = found

TABLE 1





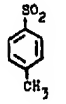
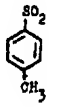
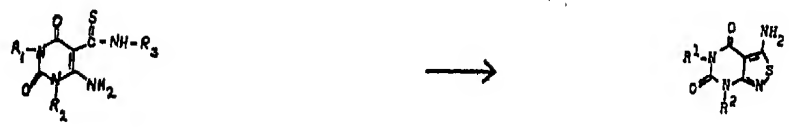
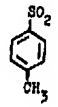
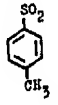
Ex	R_1	R_2	R_3	Y %	m.pt. °C	Rec.	Emp	Analysis c: f:	C %	H %	N %	O %	S %
2	H	C_2H_5		94	>330	dimethyl-formamid	$C_7H_8N_4O_2S$ 212.17		39.6 39.4	3.8 3.8	26.4 26.2	16.1 16.5	16.1
3	H	C_6H_5		99	>300	methyl-glycol	$C_{11}H_8N_4O_2S$ 260.21		50.8 50.7	3.1 3.6	21.5 21.5	12.3	12.3
4	CH_3	CH_3		95	300–306	dimethyl-formamid	$C_7H_8N_4O_2S$ 212.17		39.6 39.8	3.8 4.1	26.4 25.9	15.1 15.6	15.1 14.4

TABLE 1 (Continued)



Ex	R_1	R_2	R_3	Y %	m.pt. °C	Rec.	Emp	Analysis c: f: C %	H %	N %	O %	S %
5	C_3H_7(n)	C_3H_7(n)		97	208–210	ethanol	$C_{11}H_{16}N_4O_2S$ 268.27	49.3 49.4	6.0 6.4	20.9 20.7	11.9 12.2	11.9 11.3
6	C_4H_9(n)	C_4H_9(n)		100	166–169	ethanol	$C_{13}H_{20}N_4O_2S$ 296.32	52.7 52.5	6.8 6.9	18.9 18.7	10.8 11.2	10.8 10.4
7	CH_3	CH_3	$COOC_2H_5$	84.9	300–308	dimethyl-formamid	cf. Example 4					

Example 8.

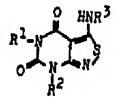
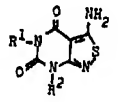
Elimination of the p-toluenesulfonyl radical:

3.66 parts of 3-[N-(p-toluenesulfonyl)]-amino - 5,7 - dimethylisothiazolo - [3,4-d]-pyrimidinedione-(4,6) is heated in 40 parts of concentrated sulfuric acid for two hours at 80° C. The cooled solution is poured onto 400 parts of ice, neutralized by adding aqueous ammonia solution, the solid material is suction filtered, washed with water and dried in vacuo at 70° C. The yield is 2.1 parts which is quantitative.

The product is identical with the compound described in Example 4.

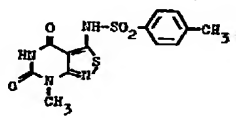
The acyl radicals in Examples 9 to 11 (set out in Table 2) may also be eliminated by the process of Example 8.

TABLE 2

Ex	R_1	R_2	R_3	Y %	m.pt. °C	Rec.	Emp. and analysis
9	CH_3	CH_3		100			as in Example 4
10	CH_3	CH_3	$COOC_2H_5$	95			as in Example 4
11	$C_4H_9(n)$	$C_4H_9(n)$		100	167–169	ethanol	as in Example 6

Example 12.

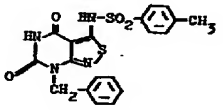


6.4 parts of bromine dissolved in 30 parts of chloroform is allowed to drip, with stirring and at 20° to 35° C, into a suspension of 7.1 parts of 3-methyl-4-aminouracil-5-[N-(*p*-toluenesulfonyl)]-carboxylic thioamide in 100 parts of chloroform. The whole is stirred for another two hours at ambient temperature and the solid is suction filtered. The product is stirred into aqueous ammonia solution, suction filtered, washed with water and dried in vacuo at 70° C. It may be recrystallized from dimethylformamide. The yield is 6.8 parts which is 97% of theory. Melting point: 300° to 305° C. Analysis: $C_{13}H_{12}N_4O_4S_2$: molecular weight: 352.26.
Calculated:

C 44.3 H 3.4 N 15.9 O 18.2 S 18.2
found:

43.9 3.5 15.4 18.3 17.9.

Example 13.

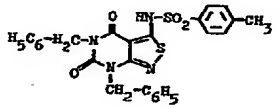


8.6 parts of 3-benzyl-4-aminouracil-5-[N-(*p*-toluenesulfonyl)] - carboxylic thioamide is cyclized as described in Example 12. The solid obtained from the chloroform solution is stirred first in a small amount of ethanol and then with aqueous ammonia solution, suction filtered, washed with water and dried. The yield is 8.5 parts which is quantitative. The melting point is 259° to 264° C. The product may be recrystallized from dimethylformamide. Analysis: $C_{19}H_{16}N_4O_4S_2$: molecular weight: 428.35.
Calculated:

C 53.1 H 3.7 N 13.2 O 15.0 S 15.0
found:

52.9 3.8 13.4 14.6 14.7.

Example 14.

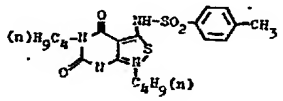


10.4 parts of 1,3-dibenzyl-4-aminouracil-5 - [N - (*p* - toluenesulfonyl)] - carboxylic thioamide is cyclized as described in Example 12. The product is precipitated from the chloroform solution by adding 100 parts of ether. It is then suction filtered, washed and dried. The yield is 10.3 parts which is quantitative. It may be recrystallized from methyl glycol. The melting point is 230° to 231° C. Analysis $C_{26}H_{22}N_4O_4S_2$: molecular weight 518.47.
Calculated:

C 60.2 H 4.3 N 10.8 O 12.3 S 12.3
found:

60.1 4.4 10.9 12.4 12.2.

Example 15.

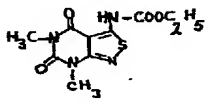


9.6 parts of bromine is dripped, while stirring and at 20° to 40° C, into 13.6 parts of 1,3 - di - *n* - butyl - 4 - aminouracil - 5-[N - (p - toluenesulfonyl)] - carboxylic thioamide in 100 parts of chloroform. The solution is stirred for another three hours at ambient temperature and then 200 parts of ether is added. The solid is suction filtered and dried in vacuo. The yield is 11.8 parts, which is 88% of theory. It can be recrystallized from methyl glycol. The melting point is 183° to 185° C. Analysis: $C_{26}H_{26}N_4O_4S_2$: molecular weight: 450.44.
Calculated:

C 53.3 H 5.8 N 12.4 O 14.2 S 14.2
found:

53.4 5.6 12.2 14.1 14.0

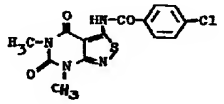
Example 16.



32 parts of bromine is dripped, while stirring and at 20° to 35° C, into 28.6 parts of 1,3 - dimethyl - 4 - aminouracil - 5-(N - carbethoxy) - carboxylic thioamide in 400 parts of chloroform. Stirring is continued for another two hours. Almost all temporarily passes into solution; gradually however a thick precipitate settles out. This is suction filtered, dissolved in about 150 parts of dimethyl formamide and then precipitated again with aqueous ammonia solution. The product is suction filtered, washed with water and dried in vacuo at 70° C. The yield is 21.4 parts or 75% of theory. The product may be recrystallized from ethanol or methyl glycol. Melting point: 143° to 145° C. Analysis: $C_{10}H_{12}N_4O_4S$; molecular weight: 284.23.

Calculated:
C 42.3 H 4.3 N 19.7 O 22.6 S 11.3
found:
42.7 4.3 19.5 23.1 10.6.

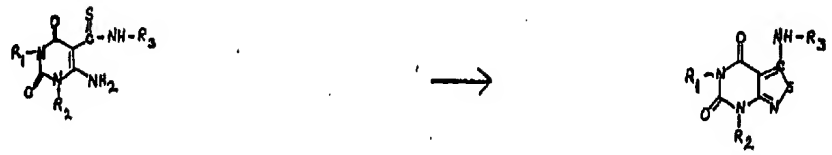
Example 17.



9.1 parts of bromine is allowed to drip at 20° to 40° C and while stirring into 10 parts of 1,3 - dimethyl - 4 - aminouracil - 5-[N - (*p* - chlorobenzoyl)] - carboxylic thioamide in 75 parts of dimethylformamide. The whole is stirred for another three hours at ambient temperature, and diluted with water, some aqueous ammonia solution is added, and the solid product is suction filtered, washed with water and dried in vacuo at 70° C. The yield is 30 parts which is 76.8% of theory. It may be recrystallized from dimethylformamide. The melting point is 246° to 250° C. Analysis: $C_{14}H_{11}N_4O_3SCl$; molecular weight: 350.7.
Calculated:
C 47.9 H 3.2 N 16.0 O 13.7 Cl 10.1
found:
48.1 3.4 15.8 13.7 10.6.

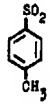
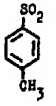
The compounds set out in Examples 18 to 24 in Table 3 may be prepared by the process described in Example 17.

TABLE 3



Ex	R_1	R_2	R_3	Y %	m.pt. °C	Rec.	Emp.	c: f:	Analysis C %	H %	N %	O %	S %
18	CH_3	CH_3		92	ab 220 Zers.	dimethyl-formamid	$C_{14}H_{12}N_4O_3S$ 316.27	c:	53.2	3.8	17.7	15.2	10.1
								f:	53.4	3.8	17.5	15.3	9.8
19	CH_3	CH_3		83.1	216–218	methyl-glycol	$C_{14}H_{14}N_4O_4S_2$ 366.28	c:	45.9	3.8	15.3	17.5	17.5
								f:	45.8	4.0	14.9	17.8	17.7
20	$C_4H_9(n)$	$C_4H_9(n)$		84	160–162	methyl-glycol	$C_{20}H_{24}N_4O_3S$ 400.42	c:	60.0	6.0	14.0	12.0	8.0
								f:	59.9	6.2	14.1	12.8	

TABLE 3 (Continued)

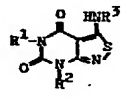
Ex	R_1	R_2	R_3	Y %	m.pt. °C	Rec.	Emp.	Analysis c: f: C %	H %	N %	O %	S %
21	$C_3H_7(n)$	$C_3H_7(n)$		76	171–173	methyl-glycol	$C_{18}H_{22}N_4O_4S_2$ 422.39	51.2 51.0	5.3 5.6	13.3 13.5	15.1 15.4	
22	H	$(CH_2)_3OCH_3$		100	268–270	dimethyl-formamid	$C_{16}H_{16}N_4O_5S_2$ 410.34	46.8 46.6	4.4 4.5	13.7 13.4	19.5 19.1	15.6 15.9
23	H	$(CH_2)_3$ | OC_2H_5		89.6	265–268	methyl-glycol	$C_{17}H_{20}N_4O_5S_2$ 424.36	48.1 47.9	4.7 4.4	13.2 13.5	18.9 18.5	14.1 13.9
24	H	$(CH_2)_3$ | $OCH(CH_3)_2$		86.5	258–261	methyl-glycol	$C_{18}H_{22}N_4O_5S_2$ 438.39	49.3 49.6	5.1 5.0	12.8 12.6	18.2 17.8	14.6 14.2

Example 25.

A mixture of 4.24 parts of 1,3-dimethyl-4 - aminouracil - 5 - [N - (*p* - toluenesulfonyl)]-carboxylic thioamide, 40 parts of dimethylformamide and 2 parts of 50% hydrogen peroxide is heated first for two hours at 50° C and then for another two hours at 100° C. The solution is cooled and water is added. The product which is precipitated is suction filtered. Chromatographically and spectroscopically it is identical with the product described in Example 21. The yield is 2.7 parts, which is 62.5% of theory.

WHAT WE CLAIM IS:—

1. A 3 - aminoisothiazolo - [3,4-d]-pyrimidine of the general formula:—



(I)

in which R^1 and R^2 are, each independently, hydrogen, a linear or branched, saturated or unsaturated alkyl group of one to six carbon atoms which optionally may be substituted, an aralkyl or an unsubstituted or substituted cycloaliphatic, heterocyclic or aromatic radical, and R^3 is hydrogen, sulfonyl or carboxylic acyl.

2. A compound as claimed in claim 1 and as individually identified in the foregoing Examples.

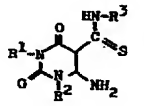
3. 3 - Amino - 5,7 - dimethylisothiazolo-[3,4-d] - pyrimidinedione - (4,6).

4. 3 - [N - Carbethoxy] - amino - 5,7-dimethylisothiazolo - [3,4-d] - pyrimidine-dione-(4,6).

5. 3 - [N - *p* - Toluenesulfonyl] - amino-7 - ethylisothiazolo - [3,4-d] - pyrimidine-dion-(4,6).

6. 3 - Amino - 5,7 - dipropylisothiazolo-[3,4-d]-pyrimidine-dione-(4,6).

7. A process for the production of a 3-aminoisothiazolo - [3,4-d] - pyrimidine as defined in claim 1 wherein a 4-aminouracil-5-carboxylic thioamide of the general formula:—



(II)

in which R^1, R^2 and R^3 are each as defined in claim 1, is oxidatively cyclized.

8. A process as claimed in claim 7 wherein the oxidative cyclization is carried out in the presence of an inert solvent and/or suspension agent at a temperature of from 0° to 180° C.

9. A compound as defined in claim 1 and whenever prepared by a process as claimed in claim 7 or claim 8.

10. A pharmaceutical composition comprising a compound as claimed in any one of claims 1 to 6 or 9 together with a pharmaceutically-acceptable carrier or diluent.

11. A fungicidal composition comprising a compound as claimed in any one of claims 1 to 6 or 9 together with a carrier or diluent.

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